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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,755	09/22/2004	Ola Junghard	1103326-0780	8288

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PATENT DEPARTMENT
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EXAMINER	
GRAHAM, SHELLEY R	
ART UNIT	PAPER NUMBER
4173	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,755	JUNGHARD ET AL.	
	Examiner	Art Unit	
	SHELLEY R. GRAHAM	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3 pages, 22 Sep 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A preliminary Amendment filed on 22 September 2002 is acknowledged. Claims 1-9 are amended, Claims 10 and 11 have been cancelled.

Claims 1-9 are under examination on the merits.

Applicant is advised that should claim 4 be found allowable, claim 5 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Objections

1. Claim 2 is objected to because of the following informalities: Claim 2 reads: "gastroesophagal reflux disease." The word "gastroesophagal" is misspelled and should read "gastroesophageal." Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ 2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claim Rejections - 35 U.S.C. § 112, 1st

3. Claims 1 and 3-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The specification does not reasonably provide enablement for treating any sleep disturbance that currently exists or may exist in the future. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

4. Claims 1 and 3-9 are drawn to a method for treatment of sleeping disturbance by administering S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-lH-benz-imidazole (esomeprazole) or a pharmaceutically acceptable salt thereof. Applicant has not defined or limited "sleeping disturbance" to any particular kind of sleeping problem. Therefore, given the broadest possible interpretation of the claims, "sleeping disturbance" is considered to include any and all forms of disorders of sleep, in which a person's sleep is disturbed.

5. The quantity of experimentation in this area is large since there is no reasonable expectation of success as the methods are not fully outlined in the specification. The examples contained in the specification are directed to the use of two self-report questionnaires, which Applicant claims "**should** be suitable for use in clinical trials of therapeutic interventions for patients with **heartburn**." According to the specification, the two questionnaires are explained as follow: the Gastrointestinal Symptom Rating Scale (GSRS) was developed to address symptoms important to patients with general gastrointestinal complaints: reflux, abdominal pain, indigestion, diarrhea, and constipation; and the Quality of Life in Reflux and Dyspepsia (QOLRAD) was developed to monitor changes in health-related quality of life in patients suffering from heartburn and dyspepsia.

6. Both tests are related to heartburn. No mention or guidance is given to how other types of "sleep disturbances," such as, but not limited to: insomnia, narcolepsy, obstructive sleep apnea, restless leg syndrome, periodic limb movement disorder, hypersomnia, circadian rhythm sleep disorders (such as delayed sleep phase syndrome, advanced sleep phase syndrome, non-24-hour sleep-wake syndrome), and parasomnias, such as, REM sleep behavior disorder, sleep terror, sleepwalking, tooth-grinding, bedwetting, sudden infant death syndrome, sleep talking,

sleep sex, and exploding head syndrome, are treated with administration of esomeprazole. The specification fails to address any of these issues.

7. The unpredictability and state of the art at the time of invention was such that treatment for sleep disorders included behavioral treatments, medications and somatic treatments. However, none of these approaches is sufficient to treat all patients with sleep disorders. Rather the choice of treatment depends on the patient's diagnosis and medical history.

8. The level of skill in the art is deemed to be high, that of PhD or MD.

9. In the instant case, as discussed above, the specification provides one with no written description or guidance that leads one to a method for treating "sleeping disorders" of any and all origin. One of ordinary skill in the art cannot readily anticipate how esomeprazole is to effect the treatment of the subject matter to which the claimed invention pertains. Thus given an art whose nature is identified as unpredictable, the lack of guidance in the specification, the large quantity of research required to determine the correct methodology to employ, the presence of no examples utilizing a working protocol, it is concluded that it would require undue experimentation for one of skill in the art to perform the method of claims 1 and 3-9 as written.

Claim Rejections - 35 U.S.C. § 103

Rejection under 35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the

subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicants are advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 2-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over COTTON et al., WO 98/54171, in view of MURPHY et al., "Sleep and the Respiratory Complications of Gastroesophageal Reflux"; *Practical Gastroenterology*, vol. 17, **1993**; pages 16-29 (already of record in Applicants IDS, 22 September 2004).

10. Claims 2-9 are drawn to a method for improving sleep in a patient suffering from gastroesophageal reflux disease comprising administering S-5-methoxy-2-[[(4-methoxy-3,5-

dimethyl-2-pyridinyl)methyl]-sulfinyl]-lH-benz-imidazole (esomeprazole) or a pharmaceutically acceptable salt thereof (claim 2).

11. Further aspects of the instantly claimed invention include the Mg^{2+}, Ca^{2+}, Na^{+}, and K^{+} forms of the salt (claim 3), with the magnesium salt being preferred (claims 4 and 5). The methods of administration claimed are orally (claim 6) and parenterally (claim 7), in a dose range from 1 mg to 100 mg daily, preferably 10 mg to 40 mg daily (claims 8 and 9).

12. The invention of COTTON et al. relates to the magnesium salt of the S-enantiomer of omeprezole trihydrate, S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]-sulfinyl]-lH-benzimidazole magnesium salt trihydrate (see Example 1 and claim 1). COTTON et al. teach a method of treating a gastric acid related condition comprising administering the magnesium salt of S-omeprazole trihydrate (claim 16), including, reflux esophagitis, gastritis, duodenitis, gastric ulcer and duodenal ulcer (see page 6, lines 2-4). Any suitable route of administration may be employed, with oral administration being preferred (see page 7, lines 1-2), but not excluding parental administration (see page 7, lines 1-2). Doses ranged from 5 mg to 300 mg, preferably 10 mg to 80 mg (see page 7, lines 19-21).

13. What COTTON et al. does not teach is the specific use of S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]-sulfinyl]-lH-benzimidazole magnesium salt trihydrate for affecting sleep.

14. MURPHY et al. teach that patients suffering from gastroesophageal reflux also suffer acid-induced arousal from sleep (see page 17, second column, last full sentence). During sleep, the coughing and protective laryngeal response to noxious stimuli, such as interesophageal acid, are not active for protecting the lower respiratory tract from aspiration.

15. The combined teachings of COTTON et al. and MURPHY et al. serve as prior knowledge that S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]-sulfinyl]-lH-benzimidazole magnesium salt trihydrate, useful for treating gastric acid related conditions, would have the effect of limiting interesophageal acid, thereby reducing arousal from sleep. Consequently, upon administration of S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]-sulfinyl]-lH-benzimidazole magnesium salt trihydrate (COTTON et al.) sleep would also be improved, thus rendering the claimed method of the instant application obvious over the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shelley R. Graham whose telephone number is 571-270-1563. The examiner can normally be reached on M-R 8 am-3 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRG
18 December 2007

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614